2018 Current Fiscal Year Report: Anesthetic and Analgesic Drug Products Advisory Committee

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1. Department or Agency	2. Fiscal Year
Department of Health and Human Services	2018
3. Committee or Subcommittee	**3b. GSA Committee No.**
Anesthetic and Analgesic Drug Products Advisory Committee	788

4. Is this New During Fiscal Year?	5. Current Charter	6. Expected Renewal Date	7. Expected Term Date
No	05/01/2018	05/01/2020	

8a. Was Terminated During FiscalYear?	8b. Specific Termination Authority	8c. Actual Term Date
No		

9. Agency Recommendation for Next FiscalYear	10a. Legislation Req to Terminate?	10b. Legislation Pending?
Continue	Not Applicable	Not Applicable

11. Establishment Authority Authorized by Law

12. Specific Establishment Authority	13. Effective Date	14. Commitee Type	14c. Presidential?
21 U.S.C. 394	11/28/1990	Continuing	No

15. Description of Committee Scientific Technical Program Advisory Board

16a. Total Number of Reports No Reports for this FiscalYear

17a. Open 4 **17b. Closed** 0 **17c. Partially Closed** 1 **Other Activities** 0 **17d. Total** 5

Meetings and Dates

Purpose	Start	End
On February 14, 2018, the Anesthetic and Analgesic Drug Products Advisory Committee met jointly with the Drug Safety and Risk Management Advisory Committee to discuss new drug application (NDA) 209257, proposed tradename, HYDEXOR, a fixed-dose combination oral tablet, submitted by Charleston Laboratories, Inc., that contains hydrocodone, acetaminophen, and promethazine, for the shortterm management of acute pain severe enough to require an opioid analgesic while preventing and reducing opioid-induced nausea and vomiting. The committees were also asked to discuss the abuse potential of this non-abuse-deterrent product and whether it should be approved.	02/14/2018	02/14/2018
On February 14-15, the committee discussed supplemental new drug application (sNDA) 022496/S-009, for EXPAREL (bupivacaine liposomal injectable suspension), submitted by Pacira Pharmaceuticals, Inc., to produce local analgesia and as a nerve block to produce regional analgesia.	02/14/2018	02/15/2018
On May 22, 2018, the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee met jointly to discuss new drug application (NDA) 209588, for buprenorphine sublingual spray, submitted by INSYS Development Company, Inc., for the treatment of moderate-to-severe acute pain where the use of an opioid analgesic is appropriate.	05/22/2018	05/22/2018

On June 26, 2018, the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee met jointly to discuss new drug application 022324, oxycodone extended-release capsules, submitted by Pain Therapeutics, with the proposed indication of the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. The product is intended to have abuse-deterrent properties based on its physicochemical properties. The committees were also asked to discuss whether the data submitted by the Applicant are sufficient to support labeling of the product with the properties expected to deter abuse.	06/26/2018 - 06/26/2018
The Drug Safety and Risk Management Advisory Committee met jointly with the Anesthetic and Analgesic Drug Products Advisory Committee to discuss results from assessments of the transmucosal immediate-release fentanyl (TIRF) medicines' risk evaluation and mitigation strategy (REMS), approved in December 2011. The TIRF REMS requires that healthcare providers who prescribe TIRF medicines for outpatient use are specially certified, that pharmacies that dispense TIRF medicines for inpatient and outpatient use are specially certified, and that completion of the prescriber-patient agreement form occurs prior to dispensing TIRF medicines for outpatient use. The Agency will seek the committees' assessment as to whether this REMS with elements to assure safe use (ETASU) assures safe use, is not unduly burdensome to patient access to the drugs, and to the extent practicable, minimizes the burden to the healthcare delivery system. The Agency will also seek the committees' input on any possible modifications to the TIRF REMS goals and requirements, as well as input on the adequacy of the evaluations conducted in the REMS assessments to determine whether the TIRF REMS goals are being met. Comments from the public can be submitted to the docket (see PUBLIC PARTICIPATION INFORMATION) on a broad evaluation of the TIRF REMS and whether any aspect of the TIRF REMS should be modified as well as any proposed modifications.	08/03/2018 - 08/03/2018

Number of Committee Meetings Listed: 5

	Current FY	Next FY
18a(1). Personnel Pmts to Non-Federal Members	$15,715.00	$39,373.00
18a(2). Personnel Pmts to Federal Members	$0.00	$0.00
18a(3). Personnel Pmts to Federal Staff	$172,271.00	$174,886.00
18a(4). Personnel Pmts to Non-Member Consultants	$12,572.00	$13,671.00
18b(1). Travel and Per Diem to Non-Federal Members	$19,349.00	$34,939.00
18b(2). Travel and Per Diem to Federal Members	$0.00	$0.00
18b(3). Travel and Per Diem to Federal Staff	$0.00	$0.00
18b(4). Travel and Per Diem to Non-member Consultants	$19,823.00	$19,161.00
18c. Other(rents,user charges, graphics, printing, mail, etc.)	$57,079.00	$57,876.00
18d. Total	$296,809.00	$339,906.00
19. Federal Staff Support Years (FTE)	1.10	1.10

20a. How does the Committee accomplish its purpose?

The Committee reviews and evaluates available data concerning the safety and effectiveness of marketed and investigational human drug products including analgesics, e.g., abuse-deterrent opioids, novel analgesics, and issues related to opioid abuse, and those for use in anesthesiology and makes appropriate recommendations to the Commissioner of Food and Drugs.

20b. How does the Committee balance its membership?

Members are authorities knowledgeable in the fields of anesthesiology, analgesics (such as: abuse deterrent opioids, novel analgesics, and issues related to opioid abuse)

epidemiology or statistics, and related specialties. The core of voting members may include one technically qualified member, selected by the Commissioner or designee, who is identified with consumer interests and is recommended by either a consortium of consumer-oriented organizations or other interested persons. In addition to the voting members, the Committee may include one non-voting member who is identified with industry interests.

20c. How frequent and relevant are the Committee Meetings?

The committee met five times in FY-18. On February 14, 2018, the Anesthetic and Analgesic Drug Products Advisory Committee met jointly with the Drug Safety and Risk Management Advisory Committee to discuss new drug application (NDA) 209257, proposed tradename, HYDEXOR, a fixed-dose combination oral tablet, submitted by Charleston Laboratories, Inc., that contains hydrocodone, acetaminophen, and promethazine, for the short term management of acute pain severe enough to require an opioid analgesic while preventing and reducing opioid-induced nausea and vomiting. The committees were also asked to discuss the abuse potential of this non-abuse-deterrent product and whether it should be approved. The majority of the committee (19 to 2) agreed that Hydexor should not be approved. Some of the committee members who voted “No” stated that their vote was based on the lack of dosing flexibility and that the ramifications of the risks associated with Hydexor did not outweigh its benefit. Overall, the majority of the committee agreed that Hydexor poses greater risks than currently marketed hydrocodone-acetaminophen products. Some committee members added that an antiemetic may not be needed for every dose of analgesic, and that a fixed-dose combination of Hydexor would expose patients to unnecessary side effects of promethazine when it is not needed. Other committee members agreed that the applicant’s proposed risk mitigation strategies are not convincing. One committee member who voted “Yes” viewed Hydexor as another opioid option and noted that its risks are no greater than what is currently on the market. Additionally, this member noted that that the population receiving Hydexor would be those who were prone to OINV and that the medication would be taken as needed. The other committee member who voted “Yes” stated that the overall benefits outweighed the risks but also suggested that toxicity data of promethazine when patients took more than six pills a day is needed. Agency Action: The Agency is still reviewing all recommendations that were made at the meeting. On February 14-15, the committee discussed supplemental new drug application (sNDA) 022496/S-009, for EXPAREL (bupivacaine liposomal injectable suspension), submitted by Pacira Pharmaceuticals, Inc., to produce local analgesia and as a nerve block to produce regional analgesia. A slight majority of the committee (6 to 4) voted “No” that the data submitted did not support approval of an additional indication for nerve block. Some of the committee members who voted “No” agreed that some efficacy was demonstrated but

had major concerns with safety. Some members who voted “Yes” also indicated that they would like to see additional studies; however, they did not specify whether these should be conducted pre- or post-marketing. Agency Action: The Agency is still reviewing all recommendations that were made at the meeting. On May 22, 2018, the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee met jointly to discuss new drug application (NDA) 209588, for buprenorphine sublingual spray, submitted by INSYS Development Company, Inc., for the treatment of moderate-to-severe acute pain where the use of an opioid analgesic is appropriate. The committees were also asked to discuss whether this product should be approved. The majority of the committee (18 to 1) voted “No”, that the benefits of Buvaya do not outweigh the risks for the indication, “the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate,” supporting approval of Buvaya. These members also agreed that although a commendable effort was made by the applicant to introduce an innovative product that may be less likely to be abused than some schedule II opioid analgesics, the factors contributing to their vote were the late onset of analgesia, and high rate of adverse events (primarily hypoxia). The committee member who voted “Yes” explained that the low abuse potential and the lack of alternative treatments available in the market were factors considered in the vote. Agency Action: The Agency is still reviewing all recommendations that were made at the meeting. On June 26, 2018, the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee met jointly to discuss new drug application 022324, oxycodone extended-release capsules, submitted by Pain Therapeutics, with the proposed indication of the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. The product is intended to have abuse-deterrent properties based on its physicochemical properties. The committees were also asked to discuss whether the data submitted by the Applicant are sufficient to support labeling of the product with the properties expected to deter abuse. The majority of the panel members (14 to 3) voted “No”, that the efficacy, safety and risk-benefit profile of Remoxy ER do not support the approval of this application. The committee members largely agreed that the public health risks of approving this reformulation of oxycodone does not outweigh its benefits. Other comments included that approving Remoxy ER with an abuse deterrent label may create a false sense of safety for this formulation and that the benefits of its nasal deterrence properties are not enough to justify approval with abuse deterrent labeling. Panelists voting “No” largely agreed that Remoxy ER did not demonstrate enough abuse deterrent properties via the oral and IV routes of administration. Of the committee members who voted “Yes,” the key comments were that the Applicant had met the standard for safety and efficacy and also met the criteria for abuse deterrence via the nasal and IV routes. On August 3, 2018, a meeting

was held jointly with the Drug Safety and Risk Management Advisory Committee. Further information regarding this meeting is provided in the Recommendation Remarks section. It is expected that this meeting will meet 5-6 times in FY-19.

20d. Why can't the advice or information this committee provides be obtained elsewhere?

Members of the committee are drawn from academia, research, and/or clinical practice. Their advice and input lends credibility to regulatory decisions made by the Agency. The alternate means of obtaining this advice would be to hire large numbers of scientists on a full time basis at great expense to the government.

20e. Why is it necessary to close and/or partially closed committee meetings?

The committee held one partially closed meeting jointly with another committee during FY-18. On June 26, 2018, from 8 a.m. to 9:30 a.m., the joint meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee was closed to permit discussion and review of trade secret and/or confidential commercial information (5 U.S.C. 552b(c)(4)). During this session, the committees will discuss the drug development program of an investigational opioid formulation with properties designed to deter abuse.

21. Remarks

This committee was not required any reporting for FY18. During FY-18, there was one meeting that this committee met in joint session with another committee, but was not the lead committee. So that joint meetings are not counted twice in the FACA database, they will be reported under the primary or lead committee. For the purposes of this database, the secondary committee still reports meeting information and costs associated under this section of the report as well as the cost section. On August 3, 2018, the Drug Safety and Risk Management Advisory Committee and the Anesthetic and Analgesic Drug Products Advisory Committee met jointly to discuss results from assessments of the transmucosal immediate-release fentanyl (TIRF) medicines' risk evaluation and mitigation strategy (REMS), approved in December 2011. The TIRF REMS requires that healthcare providers who prescribe TIRF medicines for outpatient use are specially certified, that pharmacies that dispense TIRF medicines for inpatient and outpatient use are specially certified, and that completion of the prescriber-patient agreement form occurs prior to dispensing TIRF medicines for outpatient use. The Agency sought the committees' assessment as to whether this REMS with elements to assure safe use (ETASU) assured safe use, was not unduly burdensome to patient access to the drugs, and to the extent practicable, minimized the burden to the healthcare delivery system. The Agency also sought the committees' input on any possible modifications to the TIRF REMS goals and

requirements, as well as input on the adequacy of the evaluations conducted in the REMS assessments to determine whether the TIRF REMS goals are being met. Most committee members agreed that the goals and objectives of the TIRF REMS are appropriate. Some members suggested strengthening the REMS to ensure TIRF medicines are used for cancer breakthrough pain only while others noted that patients with non-cancer breakthrough pain should be able to get them too. The committee members also recommended improving approaches to education and ensuring providers and patients have knowledge of TIRF REMS in practice. Regarding the decreased usage of TIRF medications, the committee members noted multiple explanations, including more appropriate use, changes in pharmacy benefits, cost considerations, cheaper alternative opioids, and stigma to fentanyl. The committees agreed that there are barriers, which are reasonable given the risks associated with TIRF medicines. Regarding the findings suggestive of increasing rates of adverse events, the committee members noted a number of plausible explanations, including a shift of patient population to high risk patients, more awareness of fentanyl and adverse effects leading to surveillance bias, and changes in the specific TIRF medicine being used that might have different risk profiles. The committee members also noted that the number of events are small and the estimates of risk are unstable due to sparse data, and therefore it is a challenge to come to any conclusion. Agency Action: The Agency is still reviewing all recommendations that were made at the meeting. This committee was not required any reporting for FY18."

Designated Federal Officer

Moon Hee V. Choi DFO

Committee Members	Start	End	Occupation	Member Designation
Bateman, Brian	04/01/2015	03/31/2019	Associate Professor, Harvard Medical School	Special Government Employee (SGE) Member
Brown, Raeford	04/01/2015	03/31/2019	Professor of Anesthesiology and Pediatrics, College of Medicine, University of Kentucky	Special Government Employee (SGE) Member
Craig, David	04/01/2014	03/31/2018	Clinical Pharmacy Specialist, H. Lee Moffitt Cancer Center and Research Institute	Special Government Employee (SGE) Member
Galinkin, Jeffrey	07/02/2014	03/31/2018	Professor of Anesthesiology and Pediatrics, University of Colorado, AMC, Director of Scientific and Medical Affairs, CPC Clinical Research	Special Government Employee (SGE) Member
Goudra, Basavana	04/01/2018	03/31/2022	Director of Endoscopy Anesthesia Services, Penn Presbyterian Medical Center	Special Government Employee (SGE) Member
Gupta, Anita	04/01/2016	01/05/2018	Vice Chair and Associate Professor Division of Pain Medicine & Regional Anesthesiology Department of Anesthesiology Drexel University College of Medicine	Special Government Employee (SGE) Member
Herring, William	02/29/2016	10/31/2019	Associate Vice President, Clinical Neuroscience, Merck Research Laboratories	Representative Member

Higgins, Jennifer	04/01/2014	03/31/2018	CONSUMER REPRESENTATIVE; Director of Compliance and Quality Assurance, Center for Human Development	Special Government Employee (SGE) Member
Litman, Ronald	04/01/2017	03/31/2021	Professor of Anesthesiology & Pediatrics, University of Pennsylvania	Special Government Employee (SGE) Member
McCann, Mary Ellen	05/24/2016	03/31/2020	Associate Professor of Anesthesia Harvard Medical School Senior Associate in Anesthesia Boston Children's Hospital	Special Government Employee (SGE) Member
Shoben, Abigail	06/05/2015	03/31/2019	Associate Professor, Division of Biostatistics, College of Public Health, Ohio State University	Special Government Employee (SGE) Member
Zacharoff, Kevin	04/01/2017	03/31/2021	Faculty and Clinical Instructor, Pain and Medical Ethics, SUNY Stony Brook School of Medicine	Special Government Employee (SGE) Member
Zeltzer, Lonnie	04/25/2017	03/31/2021	Distinguished Professor, David Geffen School of Medicine at UCLA	Special Government Employee (SGE) Member

Number of Committee Members Listed: 13

Narrative Description

FDA's strategic priorities in responding to the public health challenges of the 21st century are to advance regulatory science and innovation; strengthen the safety and integrity of the global supply chain; strengthen compliance and enforcement activities to support public health; expand efforts to meet the needs of special populations; advance medical countermeasures and emergency preparedness; advance food safety and nutrition; promote public health by advancing the safety and effectiveness of medical products; establish an effective tobacco regulation, prevention, and control program; and manage for organizational excellence and accountability. The Anesthetic and Analgesic Drug Products Advisory Committee supports FDA's strategic priorities by reviewing and evaluating data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of anesthesia and treatment of pain and makes appropriate recommendations to the Commissioner of Food and Drugs.

What are the most significant program outcomes associated with this committee?

	Checked if Applies
Improvements to health or safety	✓
Trust in government	✓
Major policy changes	✓
Advance in scientific research	✓
Effective grant making	
Improved service delivery	
Increased customer satisfaction	✓
Implementation of laws or regulatory requirements	✓

Other	☐

Outcome Comments
N/A

What are the cost savings associated with this committee?

	Checked if Applies
None	☐
Unable to Determine	☑
Under $100,000	☐
$100,000 - $500,000	☐
$500,001 - $1,000,000	☐
$1,000,001 - $5,000,000	☐
$5,000,001 - $10,000,000	☐
Over $10,000,000	☐
Cost Savings Other	☐

Cost Savings Comments
The utilization of the Anesthetic and Analgesic Drug Products Advisory Committee enables the Agency to obtain required and frequently scarce professional services from medical and scientific experts not otherwise available to the Agency; and to obtain the services of these experts not otherwise available to the Agency; and to obtain the services of these experts only on an as needed bases rather than on a full time basis. The service of the committee resulted in advice for the improvement of the public health, for which it is difficult to assign a financial value.

What is the approximate Number of recommendations produced by this committee for the life of the committee?
47

Number of Recommendations Comments
The Committee made 47 recommendations from FY-03 through FY-18. See question 20a of the annual report for specific accomplishments.

What is the approximate Percentage of these recommendations that have been or will be Fully implemented by the agency?
79%

% of Recommendations Fully Implemented Comments

The function of an advisory committee is purely advisory in nature. Although the FDA most often accepts the recommendations from its committees, the advice is purely advisory in nature, and therefore, the Agency has the option of not implementing the advice.

What is the approximate Percentage of these recommendations that have been or will be Partially implemented by the agency?
9%

% of Recommendations Partially Implemented Comments
The function of an advisory committee is purely advisory in nature. Although the FDA most often accepts the recommendations from its committees, the advice is purely advisory in nature, and therefore, the Agency has the option of not implementing the advice

Does the agency provide the committee with feedback regarding actions taken to implement recommendations or advice offered?
Yes ☑ No ☐ Not Applicable ☐

Agency Feedback Comments
Product approval issues are first released to the sponsor. When appropriate, information is made available to the public. Actions related to guidance documents or other general matters issues are available publicly when implemented.

What other actions has the agency taken as a result of the committee's advice or recommendation?

	Checked if Applies
Reorganized Priorities	☑
Reallocated resources	☐
Issued new regulation	☑
Proposed legislation	☐
Approved grants or other payments	☐
Other	☑

Action Comments
FDA approves or chooses not to approve new medical products.

Is the Committee engaged in the review of applications for grants?
No

Grant Review Comments

N/A

How is access provided to the information for the Committee's documentation?

	Checked if Applies
Contact DFO	☑
Online Agency Web Site	☑
Online Committee Web Site	☑
Online GSA FACA Web Site	☑
Publications	☑
Other	☐

Access Comments

N/A